

Complete Summary

GUIDELINE TITLE

Use of serum prolactin in diagnosing epileptic seizures. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology.

BIBLIOGRAPHIC SOURCE(S)

Chen DK, So YT, Fisher RS. Use of serum prolactin in diagnosing epileptic seizures: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology* 2005 Sep 13;65(5):668-75. [32 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

- Epileptic seizures, including generalized tonic-clonic seizures and complex partial seizures
- Psychogenic nonepileptic seizures
- Syncope
- Status epilepticus
- Repetitive seizures
- Neonatal seizures

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Diagnosis

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Neurology
Pediatrics

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To review the use of serum prolactin assay in epileptic seizure diagnosis

TARGET POPULATION

Adults and older children who have experienced seizures or seizure-like events

INTERVENTIONS AND PRACTICES CONSIDERED

Serum prolactin assay

MAJOR OUTCOMES CONSIDERED

- Usefulness of serum prolactin assay in differentiating epileptic seizures from psychogenic non-epileptic seizures
- Effect of other neurologic changes (e.g., syncope, repetitive seizures, and neonatal seizures) on serum prolactin levels.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline authors searched MEDLINE, Science Citation Index, and the Cochrane Database, combining the search term prolactin with the terms seizure(s), pseudoseizure(s), epilepsy, syncope, or status epilepticus. Three hundred ninety-six articles were identified as of March 2005. The abstracts of these articles were reviewed, specifically looking for controlled studies that reported on prolactin (PRL) changes following seizures or seizurelike events.

Reviews without original data, letters, meeting abstracts, and case reports/series were excluded.

The guideline authors examined 41 articles in their entirety, along with 5 additional articles identified upon reviewing bibliographies of the retrieved articles. Three articles in German were translated into English. The articles were categorized into two groups: Group 1 consisted of controlled studies investigating the use of postevent PRL to discriminate epileptic seizures (ES) from psychogenic nonepileptic seizures (NES). Group 2 consisted of controlled studies assessing serum PRL changes following syncope, repetitive seizures, or neonatal seizures. For Group 1, studies were selected for inclusion into the analysis based on the following criteria: 1) prospective design, 2) implementation of reference standard in the form of continuous electroencephalogram (EEG) monitoring, 3) specification of the threshold for PRL elevation and the postevent lapse time of PRL measure, 4) reporting of the accuracy rates of PRL assay among case and control groups, and 5) publication in a peer-reviewed journal. For Group 2, all published studies that prospectively investigated serum PRL changes following tilt-induced and monitored syncope, repetitive seizures, status epilepticus (SE), or neonatal seizures were included. Wherever a study reported more than one criterion for elevated PRL, the authors analyzed the data arising from criterion closest to the common criteria chosen by other studies of the same group (i.e., twice baseline level, or > 36 ng/mL for Group 1). PRL measures presented in uU/mL or ug/L were converted for consistency of presentation to ng/mL.

NUMBER OF SOURCE DOCUMENTS

46 articles were reviewed

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Class I: Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a reference ("gold") standard for case definition, where a test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. All patients undergoing the diagnostic test have the presence or absence of the disease determined.

Class II: Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared with a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where the

reference standard, if not objective, is applied by someone other than the person who performed the test.

Class IV: Any design where the test is not applied in an independent evaluation or evidence provided by expert opinion alone or in descriptive case series (without controls).

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Most laboratories report prolactin (PRL) upper normal limits of 18 to 23 ng/mL. However, prior literature does not specify a precise and commonly accepted cutoff PRL level as an indicator of epilepsy. The authors accepted the individual investigators' opinion of abnormal PRL elevation. From the proportion of elevated PRL for each seizure type reported, the authors calculated sensitivity and specificity, where appropriate. Ninety-five percent confidence intervals (CIs) for each parameter were calculated using the Wilson score method without continuity correction. From all Class I and Class II studies, the sensitivity values were then pooled by calculating the weighted average. The same process was performed for the specificity values. Applying Bayes' theorem, the positive or negative predictive values of serum PRL assay would depend not only on the sensitivity and specificity parameters, but also on the pretest probability that an event is epileptic. The authors calculated the predictive values for a range of epileptic seizures pretest probabilities from 99% to 50%, assuming the respective pooled sensitivity and specificity for generalized tonic-clonic seizures, complex partial seizures, and all epileptic seizures combined.

The authors set the requirement that both patient sample size and number of seizures studied must be 50 or greater for a study to be considered "wide spectrum" for the purpose of evidence classification. The varieties of seizure types studied were also weighed in assessing extent of patient spectrum.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

A: Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)

B: Probably effective, ineffective, or harmful for the given condition in the specified population. (Level B rating requires at least one Class I study or at least two consistent Class II studies.)

C: Possibly effective, ineffective, or harmful for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U: Data inadequate or conflicting given current knowledge; treatment is unproven.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This guideline was approved by the Therapeutics and Technology Assessment Subcommittee on November 19, 2004; by the Practice Committee on April 13, 2005; and by the Board of Directors on June 25, 2005.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions of the classification of the recommendations (A, B, C, U) and classification of the evidence (Class I through Class IV) are provided at the end of the "Major Recommendations" field.

Practice recommendations: For clinicians considering a laboratory blood test to diagnose epileptic seizures (ES)

1. Elevated serum prolactin (PRL), when measured in appropriate clinical setting at 10 to 20 minutes after a suspected event, should be considered a useful adjunct to differentiate generalized tonic-clonic seizures or complex partial seizures from psychogenic nonepileptic seizures among adults and older children (Level B).
2. Serum PRL, when measured more than 6 hours after a suspected event, should be representative of the baseline PRL level (Level B).
3. Serum PRL assay is not of utility to distinguish seizure from syncope (Level B).
4. The utility of serum PRL assay has not been established in the evaluation of status epilepticus, repetitive seizures, or neonatal seizures (Level U).

Definitions

Classification of Recommendation

A: Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)

B: Probably effective, ineffective, or harmful for the given condition in the specified population. (Level B rating requires at least one Class I study or at least two consistent Class II studies.)

C: Possibly effective, ineffective, or harmful for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U: Data inadequate or conflicting given current knowledge; treatment is unproven.

Classification of Evidence

Class I: Evidence provided by a prospective study in a broad spectrum of persons with the suspected condition, using a reference ("gold") standard for case definition, where a test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy. All patients undergoing the diagnostic test have the presence or absence of the disease determined.

Class II: Evidence provided by a prospective study of a narrow spectrum of persons with the suspected condition, or a well-designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared with a broad spectrum of controls, where test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.

Class III: Evidence provided by a retrospective study where either persons with the established condition or controls are of a narrow spectrum, and where the reference standard, if not objective, is applied by someone other than the person who performed the test.

Class IV: Any design where the test is not applied in an independent evaluation or evidence provided by expert opinion alone or in descriptive case series (without controls).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate and effective use of serum prolactin assay to differentiate epileptic seizures from psychogenic nonepileptic seizures

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This assessment focused on the use of serum prolactin assay in the diagnosis of epileptic seizures. The utility of serum prolactin assay in other indications is beyond the scope of this review. This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The American Academy of Neurology recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads
Slide Presentation

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Sep

GUIDELINE DEVELOPER(S)

American Academy of Neurology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Neurology (AAN)

GUIDELINE COMMITTEE

Therapeutics and Technology Assessment Subcommittee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The authors report no conflicts of interest.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the [AAN Web site](#).

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 1080 Montreal Avenue, St. Paul, MN 55116.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Use of serum prolactin in diagnosing epileptic seizures. St. Paul (MN): American Academy of Neurology. 2005. 12 p. Available for personal digital assistant (PDA) download from the [American Academy of Neurology \(AAN\) Web site](#).
- Use of serum prolactin in diagnosing epileptic seizures slide presentation. St Paul (MN): American Academy of Neurology. Available from the [AAN Web site](#).
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the [AAN Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on December 23, 2005.

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